REMARKS

The pending claims have been rejected under 35 U.S.C. § 112 ¶¶ 1 and 2. Paragraph 2 (page 6 of the Office Action) will be addressed first.

The first point made in the § 112, ¶ 2 rejection is that the elected claims are indefinite because they are not limited to the treatment of stroke, but rather encompass "treating any disorder of the central nervous." Applicants have not amended the claims in response to this ground of rejection; Applicants submit that the phrase "improvement in function of the central nervous system" is definite and can be readily understood by any person of ordinary skill in the art. The restriction requirement, which was traversed, does not render the phrase indefinite.

The second ground of rejection for indefiniteness has been met by the amendment to claim 1, which now requires that the aliquot of cells be administered "in an amount sufficient to cause said improvement."

The rejection under 35 U.S.C. § 112 first paragraph, for overbreadth, is respectfully traversed.

The Office Action states that "the specification, while being enabling for a method of causing improvement in function of the central nervous system in a mammal having a brain ischemia resulting from stroke, comprising injecting CD34+/-, Lin-cells into an ischemic region of the mammal's brain, does not reasonably provide enablement for the various methods of treating covered by the claims." The primary basis for this rejection is the fact that the working example is limited to the above-characterized method. The

Office Action further states that "the specification does not teach how to use the claimed methods to produce a therapeutic effect over the full scope of the claim..."

At the outset, Applicants point out that a new claim, claim 44, combines the limitations of claims 1, 18, and 26, and is of the scope deemed patentable in the Office Action, except for the claim's omission of a recitation of a mode of cell delivery. New claim 45, which depends from new claim 44, requires that the cells be delivered to the affected region of the brain or intravenously, while new claims 46 and 47 require that the cells be delivered to the affected region of the brain.

Turning now to the rejection for claim overbreadth under 35 U.S.C. § 112, ¶ 1, Applicants respectfully traverse this rejection.

The Examiner is correct in stating that "the working example is limited to transplantation of a specific cell type...into a rat that serves as a stroke model." In that example, cells were injected directly into the brain. It does not follow that the claims should be limited to what is described in the example. A bedrock tenet of patent law is that, generally, the claims should not be limited to the parameters of an example, if the specification is broadly enabling beyond the example. Such is the case here.

The Office Action states that "the specification does not teach how to use the claimed methods to produce a therapeutic effect over the full scope of the claim, which covers transplantation of a variety of cell types as well as combined administration of cells and growth factors." The Office Action goes on to state that "the specification does not offer adequate guidance," and that, because of unpredictability in the art, the

specification does not enable the practice of the invention "over the full scope" of the claims. In support of these assertions, the Office Action points out that the 1995 Jackowski et al. reference "details the limitations and unpredictability associated with transplantation of neural tissue." For the reasons given below, the rejection should be withdrawn.

First, it is not the case that the specification does not teach how to use the invention, as claimed in independent claims 1 and 37. Claim 1, moreover, is quite narrow is some respects. The only cells that are used according to the method of claim 1 are umbilical cord blood cells; there is no attempt in claim 1 to expand the cell population beyond that very specific cell type. Thus the discussion of the lack of knowledge about various different cell types (page 4 of the Office Action), and the point that Jackowski makes about unpredictability of transplantation of neural tissue, are irrelevant: Claim 1 uses cells of only one type, and those cells are not neural cells. Claim 37, which did more broadly define the cells to be used, has been amended such that it, like claim 1, is now limited to cord blood cells. The cells of independent claims 2 and 3 are also narrowly defined, and are not neural cells. Claim 2 uses stem cells, which at the time of the filing of the application were well characterized in hundreds of scientific articles and numerous patents. The same is true for the cells of claim 3, which are cells derived from blood.

With respect to the growth factors recited in several of the claims, they are all publicly available, and were well characterized at the time of the filing of the application. On page 3 of the specification, lines 21-23, Applicants list a number of well-

characterized growth factors.

The specification also provides ample guidance with respect to the cause of the impaired central nervous system function to be treated by the methods of the invention: on page 4 of the specification, lines 8 and 9, the disease states, all of which were known and thoroughly studied prior to the filing of the application, are listed. In addition, claim 28, which lists seven diseases, has been cancelled.

The specification also provides enabling guidance with respect to the dosage of cells used to according to the invention (page 6, lines 11-14), and enabling guidance as to the dosage of the growth factor to be used according to the methods of the invention (page 9, lines 3-11).

With respect to the mode of administration of the cells, suitable methods are listed in enabling detail in the specification, page 6, lines 1-6.

Significantly, since the filing of the application, a method described in the specification that was not set out in the Example has been used successfully. Attached hereto is a declaration from one of the inventors, Dr. Seth Finklestein, describing that method. Panel A of the attachment to the declaration shows the protocol used for the intravenous injection of umbilical cord blood cells together with a growth factor, dFGF, into rats one day after the induction of a stroke. As is shown in panels B and C, the treated animals exhibited significant recovery of function compared to the untreated animals. Panel D shows that the umbilical cord cells that were administered intravenously migrated to the stroke area in the brain.

Thus, it is clear that at least one method described in the specification other than the method described in the Example does, in fact, succeed in improving CNS function, just as stated in the specification.

In view of the above, it is submitted that all of the claims are in condition for allowance and such action is requested.

If there are any charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

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Susan M Michaud

Paul T. Clark
Reg. No. 30,162

Susan M. Michaud
Reg. No. 42,885

Clark & Elbing LLP
101 Federal Street
Boston, MA 02110
Telephone: 617-428-0200
Facsimile: 617-428-7045

Version of Claims Showing Changes Made

1. (Twice Amended) A method of causing an improvement in function of the central nervous system of a subject having impaired central nervous system function, comprising

a. preparing an aliquot of cells containing a predetermined target population by providing a starting sample of cells derived from umbilical cord blood, and causing cells of the target population in the starting sample to divide; and

b. administering to the subject the aliquot of cells, in an amount sufficient to cause said improvement.

37. (Twice Amended) A method of causing an improvement in central nervous system function of a patient comprising:

obtaining an aliquot containing a [predetermined target population of] cells by

(d) introducing a starting sample of cord blood cells into a growth medium;

(e) causing said cord blood cells [of the predetermined target population] to divide; and

(f) concurrently with, intermittently during, or following step (b), contacting the cells in the growth medium with a selection element comprising so as to select cells of the target population from other cells in the growth medium; and

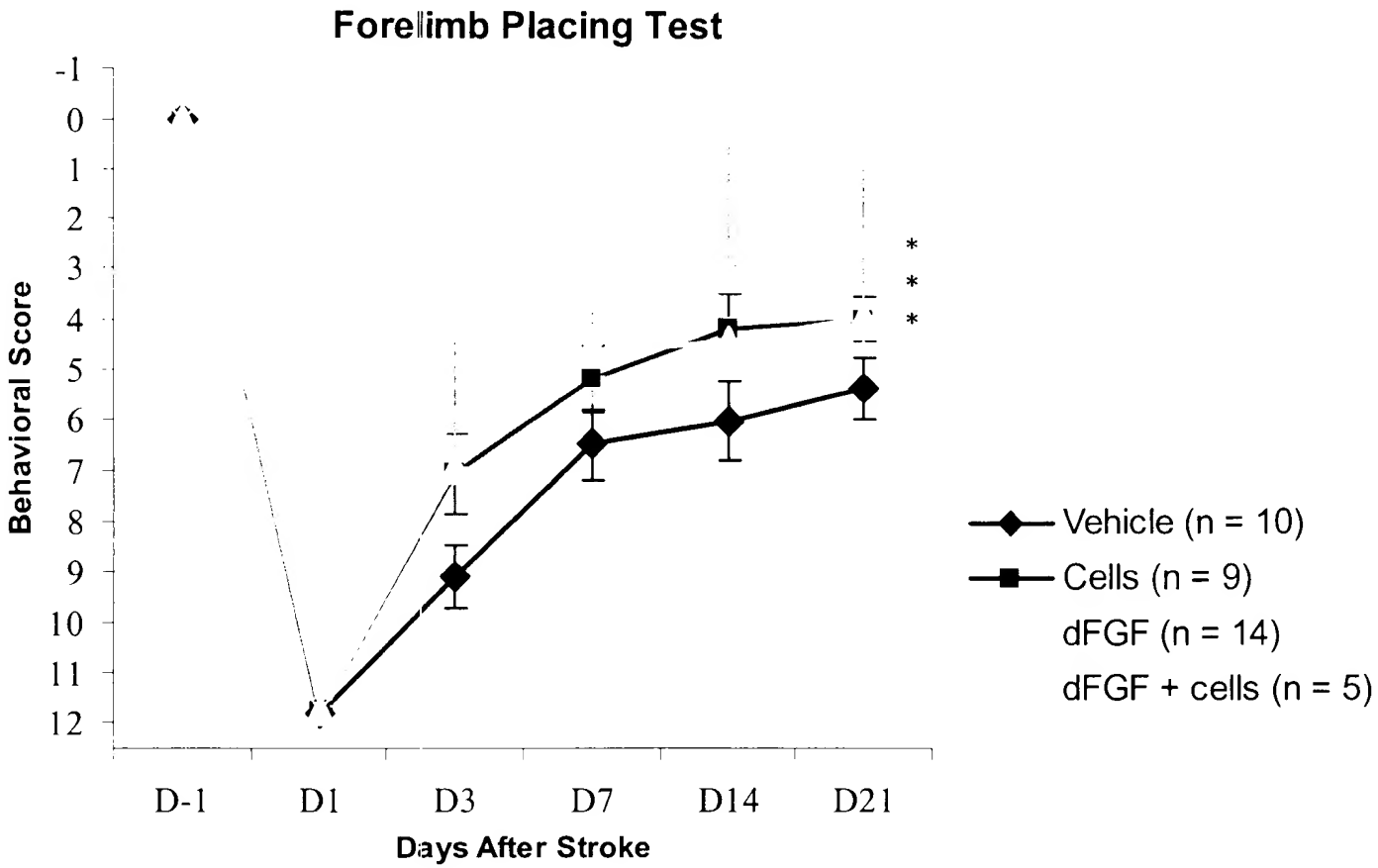
administering the aliquot to the patient.

PANEL A

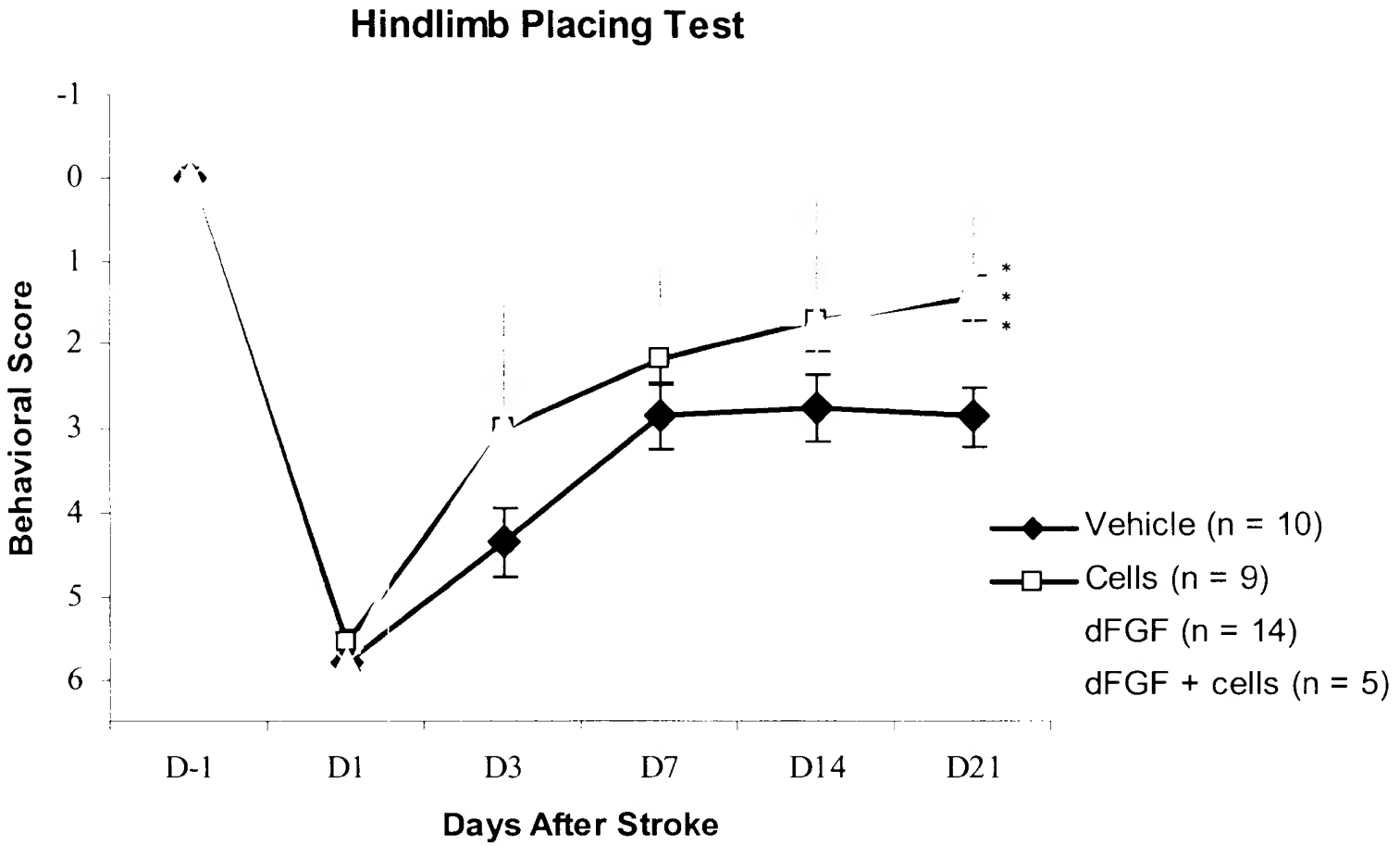
Experimental Protocol

- Unilateral strokes made in mature rats
- One day after stroke, rats received intravenously, either:
  - Vehicle
  - dFGF
  - Selectively Amplified HUCB cells
  - dFGF + HUCB cells
- Behavior examined for 3 wks. after stroke

dFGF and/or HUCB Cells Enhance Recovery of Forelimb Function After Stroke



dFGF and/or HUCB Cells Enhance Recovery of Hindlimb Function After Stroke



HUCB Cells Migrate into Stroke Area